Cortical motor and somatosensory representation: effect of cerebral lesions

RICHAIRD G. BITTAR, M.B., B.S., ANDRÉ OLIVIER, M.D., PH.D., F.R.C.S.(C),
ABBAS F. SADIROT, M.D., PH.D., F.R.C.S.(C), FREDERICK ANDERMANN, M.D., F.R.C.P.(C),
AND DAVID C. REUTENS, M.D., F.R.A.C.P.

Montreal Neurological Institute and Hospital, Montreal, Quebec, Canada; Department of Neurology and
Neurosurgery, McGill University, Montreal, Quebec, Canada; Department of Anatomy and Histology,
The University of Sydney, Sydney, New South Wales, Australia; and Department of Neurology, Austin and
Repatriation Medical Centre, Heidelberg, Victoria, Australia

Object. Changes in cortical representation in patients with cerebral lesions may alter the correlation between cortical anatomy and function. This is of potential clinical significance when the extent of cortical resection is based on surface anatomical landmarks.

Methods. Fifty-one patients with supratentorial lesions were studied. Nineteen harbored noncentral lesions (no involvement of pre- or postcentral gyrus), whereas 32 had central lesions. Control studies consisted of stimulation of the hand contralateral to the unaffected hemisphere. Positron emission tomography activation studies were performed using the $^{15}$O$\mathrm{H}_2\mathrm{O}$ tracer. Somatosensory stimulation of the hand or foot was performed using a mechanical vibrator. Motor activation consisted of hand clenching or foot tapping. The t-statistic volumes were generated from images showing the mean change in regional cerebral blood flow, and coregistered with a T$^1$-weighted magnetic resonance image. At the threshold selected, exclusive contralateral primary sensorimotor cortex activation was elicited in 100% of the control studies. A different pattern of cortical activation was associated with central lesions in 35 (78%) of 45 patients, which occurred significantly more often than with noncentral lesions (eight [31%] of 26 patients). The most common difference in the pattern of activation with central lesions was activation of cortical regions outside the central area (including the supplementary sensorimotor area and the secondary somatosensory cortex). No sensorimotor activation was observed in gyri adjacent to the pre- or postcentral gyrus.

Conclusions. Central lesions are more frequently associated with altered patterns in activation than lesions in noncentral locations. Characteristic patterns include activation of secondary sensorimotor areas. The absence of activation in gyri adjacent to the sensorimotor strip has clinical significance for the planning of resections in the central area.

KEY WORDS • motor cortex • somatosensory cortex • plasticity • tumor • epilepsy • positron emission tomography

A CONSIDERABLE amount of evidence supports the capacity of the central nervous system to adapt or “modify its own organization and function.”1 This has been most widely studied within the motor and sensory systems in which there have been a variety of lesions involving the cerebral cortex and ascending and descending pathways. Reorganization of cortical somatosensory or motor representation may occur in response to various cortical insults and abnormalities, including infarction, dysplasia, neoplasia, and vascular malformations.3–11,18,22,26,27 Changes in cortical representation in patients with cerebral lesions are of potential clinical significance when the extent of cortical resection is based purely on surface anatomical landmarks. Information on changes in representation is available in small numbers of patients with acute

Abbreviations used in this paper: MR = magnetic resonance; PET = positron emission tomography; SD = standard deviation; SII = secondary somatosensory cortex; SSMA = supplementary sensorimotor area.

and subacute lesions. For example, in response to neoplastic and ischemic lesions located in the hand area of the motor cortex in humans, hand movements may activate other parts of the precentral gyrus, the supplementary motor area, and the parietal cortex.2,26,27 By studying a large number of patients undergoing neurosurgery in which $^{15}$O$\mathrm{H}_2\mathrm{O}$ PET scanning was used, we aimed to examine patterns of motor and somatosensory organization in the presence of subacute and chronic lesions involving the primary motor and somatosensory cortices.

Clinical Material and Methods

Fifty-one patients (28 male and 23 female; age range 8–73 years) admitted to the Montreal Neurological Hospital for evaluation before planned resective surgery were involved in this study. Twenty-one patients harbored supratentorial neoplastic lesions, and 30 were evaluated for resection of noneploial epilepsymogenic lesions. The precise characteristics of the patients’ lesions are listed in Table 1.
Motor and somatosensory cortex representation

The patients were divided into two groups, based on the location of the lesion in relation to the primary sensorimotor cortex. The first group consisted of 19 patients with noncentral lesions that did not arise from or compress the pre- or postcentral gyrus. The second group consisted of 32 patients with central lesions that directly involved or compressed the pre- or postcentral gyrus. Control studies were performed in 16 of the 51 patients; these studies focused on motor or somatosensory activation of the hand contralateral to the unaffected hemisphere.

Patients were also classified according to their age when the lesion developed. Perinatal lesions, originating at or before birth, mainly consisted of cortical dysplasia and porencephaly. Lesions acquired after birth were categorized according to whether any of the acquired events were clearly evident, the onset of symptoms (as in the case of tumors).

Anatomical MR Imaging and Coregistration of PET and MR Imaging

In all patients a T1-weighted anatomical MR image (TR 18 msec; TE 10 msec; flip angle 30°) was acquired, yielding approximately 160 sagittal images, each composed of 256 × 256 1-mm³ voxels. Magnetic resonance and PET images were mapped into a common standard (stereotactic) space, by using an automated algorithm that maximized the cross-correlation between the images and the average of more than 300 normal MR images manually registered into the coordinate space of Talairach and Tournoix.24,28,29 Coregistration of PET and MR images was performed using the cross-correlation algorithm, which allowed accurate anatomical localization of the PET activation focus.

Positron Emission Tomography Scanning

Positron emission tomography scans were obtained using a scanner (model HR+ PET scanner; CTI/Siemens, Knoxville, TN) that produces 63 slices at an intrinsic resolution of 4.2 × 4.2 × 4 mm. A head mould was fitted to each patient to minimize head movement, and all scanning sessions were performed in a quiet darkened room with the patients’ eyes closed. A ⁶⁷Ge orbiting rod transmission source was used for attenuation correction.

Bolus 10-mCi intravenous injections of the cerebral blood flow tracer [¹⁵O]H₂O were administered during activation and baseline states. In each patient, two baseline scans were obtained while the patient was relaxed, and two additional scans were obtained for each activation condition. During activation scanning, vibrotactile stimulation commenced 30 seconds before injection of the tracer. Somatosensory stimulation was provided by a mechanical vibrator (model 91; Daito, Osaka, Japan) at a frequency of 110 Hz and an amplitude of 2 mm. A set of standard stimulation sites was used over the palmar surface of the fingers and the plantar surface of the foot. Motor activation consisted of self-paced (1–2 Hz) repetitive hand clenching or foot tapping. The choice of sites stimulated in each patient was dependent on the location of the lesion and the operative approach being considered. Patients were observed closely for motor activity in limbs other than those tested, which would have confounded the results. Data from studies during which other limbs were moved were discarded. The maximum number of scans was limited to 12 by patient tolerance and by the dose of radiation allowed by institutional and national guidelines.

In each of the 19 patients with noncentral lesions, 35 activation studies were performed (14 hand motor, 16 hand somatosensory, two foot motor, and three foot somatosensory studies). Sixty-two activation studies were performed in the 32 patients with central lesions (19 hand motor, 30 hand somatosensory, five foot motor, and eight foot somatosensory studies). Twenty-four control studies (motor or somatosensory activity confined to the hand ipsilateral to the lesion) were completed in 16 patients (13 motor and seven somatosensory studies).

Informed consent was obtained from each patient beforehand, and the study protocol was approved by the Research Ethics Committee of the Montreal Neurological Institute.

Statistical Parametric Mapping

For each activation condition, t-statistic volumes were generated based on images revealing the mean change in regional cerebral blood flow by dividing each voxel by the average SD pooled across voxels.³

Analysis and Interpretation

Activation peaks of a magnitude previously demonstrated³ always correlate with positive responses from direct electrical stimulation of the cerebral cortex (t ≥ 4.75) were identified, and their anatomical locations were determined. Activation patterns derived from stimulation of the hand contralateral to the unaffected hemisphere in 16 patients were used as controls. After examining the control studies, atypical patterns of activation were defined in the following manner: 1) atypical location of primary motor or somatosensory cortex activation (nonmechanical displacement); 2) recruitment of other cortical regions not seen with stimulation of the unaffected limb in individual patients, such as the SSMA and the SII; and 3) activation of ipsilateral primary sensorimotor cortex. Nonmechanical displacement of primary motor or somatosensory cortex was defined as the peak somatosensory activation located on the precentral gyrus or motor activation on the postcentral gyrus. The location of the central sulcus on the anatomical MR image was ascertained using three previously described anatomical guidelines: 1) the superior or frontal sulcus was identified in the axial plane, and its intersection with the precentral sulcus was used to locate the central sulcus;³ 2) the indentation of the cortical surface located immediately posterior to the central sulcus by

<table>
<thead>
<tr>
<th>TABLE 1</th>
<th>Nature of lesions in 51 patients</th>
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<tbody>
<tr>
<td>Type of Lesion</td>
<td>No. of Patients</td>
</tr>
<tr>
<td>neoplastic</td>
<td>21</td>
</tr>
<tr>
<td>cortical dysplasia</td>
<td>9</td>
</tr>
<tr>
<td>posttraumatic</td>
<td>6</td>
</tr>
<tr>
<td>perinatal infarction</td>
<td>4</td>
</tr>
<tr>
<td>Rasmussen’s encephalitis</td>
<td>2</td>
</tr>
<tr>
<td>cavernous hemangioma</td>
<td>2</td>
</tr>
<tr>
<td>other</td>
<td>7</td>
</tr>
</tbody>
</table>
the marginal ramus of the cingulate sulcus was useful in identifying the paracentral lobule; 3) a posterior-pointing knob, which characteristically possessed an omega shape on axial sections and a hooklike configuration in the sagittal plane, was identified on the precentral gyrus. We chose not to use the technique described by Seitz, et al., who estimated mechanical displacement by superimposing a reflection of the opposite central sulcus, because such a method is affected by asymmetry of these sulci in normal conditions.

Results

Study of Unaffected Hemisphere

Sixteen patients underwent 24 control studies. Significant activation foci were observed in 16 (67%) of these studies (Fig. 1). Of the 16 successful studies, exclusive contralateral primary sensorimotor cortex activation was elicited in 100%. Eleven of these studies were hand motor activation; contralateral activation was located in the precentral gyrus in nine cases and in the central sulcus in two cases. Of the five successful somatosensory studies, four were located in the contralateral central sulcus and one in the contralateral precentral gyrus. The latter study was classified as atypical (one [6%] of 16 studies). Activation of cortical areas other than the primary sensorimotor cortex was not observed.

Studies of Lesions

Cortical activation was analyzed with respect to the location of the lesion, patient age when the pathological entity developed, patient sex, duration of symptoms, nature of the underlying disease, and presence or absence of impaired motor or somatosensory function. Atypical activation was encountered more frequently in studies of central and noncentral lesions than in control studies (p < 0.001).

Noncentral Lesions. Nine (26%) of 35 studies failed to produce discernible activation foci. Of the 26 successful studies, activation was observed exclusively within the contralateral primary sensorimotor cortex in 18 (69%). In addition to the primary sensorimotor cortex, activation of cortical areas was observed in eight (31%) of the 26 studies (Table 2). All cases of hand motor and somatosensory activation were located either within or immediately adjacent to the precentral knob described by Yousry, et al.

Central Lesions. Forty-five (73%) of 62 studies produced significant activation foci (Fig. 2). Of the 45 successful studies, activation was normally located exclusively within the contralateral primary sensorimotor cortex in 10 (22%). Atypical cortical activation was associated with lesions in the central region in 35 (78%) of the successful studies, which was significantly more often than that found with noncentral lesions (eight [31%] of 26 studies). In addition to the contralateral primary sensorimotor cortex, other areas of activation were observed in 21 (47%) of the 45 studies (Table 3), including one case of ipsilateral primary motor cortex activation in a patient who sustained a perinatal cerebrovascular accident. Activation of areas other than the primary sensorimotor cortex was registered in seven (16%) of the 45 studies (Table 4). In six cases (13%), peak primary motor cortex activation was located on the postcentral gyrus or somatosensory activation on the precentral gyrus (three motor and three somatosensory; two cases of perinatal infarction, one case of cortical dysplasia, and three cases of neoplasm). All hand motor–activation foci in the primary motor cortex were within

<table>
<thead>
<tr>
<th>Stimulation</th>
<th>Areas Activated</th>
<th>No. of Studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>somatosensory</td>
<td>contralat parietal operculum/insula (SII)</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>contralat medial frontal lobe (SSMA)</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>ipsilat parietal operculum/insula (SII)</td>
<td>2</td>
</tr>
<tr>
<td>motor</td>
<td>contralat medial frontal lobe (SSMA)</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>contralat parietal operculum/insula (SII)</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>ipsilat medial frontal lobe (SSMA)</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>ipsilat cingulate sulcus</td>
<td>1</td>
</tr>
</tbody>
</table>

* Four (31%) of 13 somatosensory studies and four (31%) of 13 motor studies resulted in activation of areas in addition to primary sensorimotor cortex.
or immediately adjacent to the aforementioned knob. In one patient, primary somatosensory cortex activation was clearly noted on the postcentral gyrus but 1.5 cm medial to its expected location adjacent to the precentral knob. Other Variables

We found no statistically significant relationship between the occurrence of atypical activation patterns and the age of the patient at lesion onset (mean 16.3 years, SD 20.4 years with typical activation; mean 23 years, SD 22.2 years with atypical activation), patient sex, duration of symptoms (in the group with acquired lesions), or functional impairment (p < 0.05). A comparison of patients with cortical dysplasia and those with tumors also failed to demonstrate a significant difference in the prevalence of plasticity (p < 0.05).

Discussion

Using PET, we studied the patterns of cortical motor and somatosensory activation in 51 patients with supratentorial lesions. We demonstrated that there was a more frequent occurrence of altered patterns of activation in patients with cortical lesions than in control patients (p < 0.05). Cortical lesions in the central region were most closely associated with activation of secondary motor and somatosensory areas and a nonmechanical shift in peak primary sensorimotor cortex activation. The dorsoventral location of hand motor and somatosensory activation within the pre- and postcentral gyri was remarkably consistent. Furthermore, no cases of activation were observed in gyri adjacent to the anatomically described primary sensorimotor cortex.

Alterations in Cortical Somatosensory and Motor Representation

Previous investigations of motor and somatosensory representation in patients with cortical mass lesions have provided evidence of changes in the pattern of sensorimotor organization. Extensive unilateral cerebral damage in utero results in a substantial reorganization of primary motor and somatosensory cortices, and functional recovery may be associated with control of motor function by the intact hemisphere through direct ipsilateral corticospinal projections. Recovery from a motor deficit caused by an ischemic cerebrovascular accident may be accompanied by the recruitment of additional sensorimotor areas, bilateral activation of motor pathways, or enlarge-
TABLE 3
Activation of areas in addition to contralateral primary sensorimotor cortex in patients with central lesions*

<table>
<thead>
<tr>
<th>Stimulation</th>
<th>Areas Activated</th>
<th>No. of Studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>somatosensory</td>
<td>contralat parietal operculum/insula (SII)</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td>ipsilat parietal operculum (SII)</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>contralateral precuneus (Area 7)</td>
<td>1</td>
</tr>
<tr>
<td>motor</td>
<td>contralateral medial frontal lobe (SSMA)</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>ipsilat medial frontal lobe (SSMA)</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>contralateral insula (SII)</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>ipsilat parietal operculum (SII)</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>contralateral frontal operculum</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>contralateral precuneus (Area 7)</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>contralateral superior parietal lobule</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>ipsilateral central sulcus (motor cortex)</td>
<td>1</td>
</tr>
</tbody>
</table>

* Eleven (42%) of 26 somatosensory and 10 (53%) of 19 motor studies resulted in activation of areas in addition to primary sensorimotor cortex.

Patterns of Altered Cortical Organization

Recruitment of Secondary Motor and Somatosensory Areas. Activation of secondary motor and sensory cortical areas has been demonstrated following peripheral deafferentation or deafferentation, hemispherectomy (unpublished data), stroke, and cortical mass lesions. Motor activation studies performed in the current series frequently resulted in secondary sensorimotor cortex activation. Such activation was seen in four (31%) of 13 motor studies performed in patients with noncentral lesions and in 13 (68%) of 19 such studies performed in patients with central lesions. These areas consisted of the SII, the frontal operculum, and the premotor area. Similarly, somatosensory stimulation in 15 (58%) of 26 studies in patients with a central lesion produced activation of the SII, the SSMA, or the frontal operculum. Previous studies performed in healthy volunteers demonstrated activation of the SII and SSMA. In our study, these sites achieved t-statistics greater than the set threshold in individual patients but not in control studies, indicating that there was stronger activation in patients who had lesions.

Nonmechanical Displacement of Motor or Somatosensory Activation. Primary somatosensory activation localized to the precentral gyrus or motor activation localized to the postcentral gyrus was found more frequently in studies of patients with central lesions (six [13%] of 45 studies) than in control studies (one [6%] of 16 studies) (p < 0.05). This phenomenon was described by Penfield and Rasmussen, who studied responses to electrical stimulation of the cerebral cortex in patients undergoing surgery for seizures. They found that, with respect to the cortex surrounding the central sulcus, 75% of the points yielding somatosensory responses were postcentral and 25% precentral. Similarly, 20% of the points giving rise to motor responses when stimulated were postcentral, and these were not abolished by removal of the precentral gyrus. Using direct cortical stimulation with subdural electrodes in patients with epilepsy, Nii, et al., found that 27% of hand motor responses were elicited by stimulating the area posterior to the central sulcus. We also observed this phenomenon in three (20%) of 15 hand motor studies performed in patients with central lesions but not in studies performed in patients with noncentral lesions or in studies of the unaffected hemisphere. Predominant activation of the postcentral gyrus by motor activity may reflect: 1) the ability of the normal primary somatosensory cortex to subserve motor function when the primary motor cortex is dysfunctional; 2) the known extension of the primary motor cortex onto the deeper portion of the posterior wall of the central sulcus; or 3) a true functional or structural reorganization.

Methodological Considerations

The anatomical landmarks used in this study, in particular the central sulcus and precentral knob, were those identified during surgery in the region of the sensorimotor strip. These landmarks could be readily identified and, if displaced by a mass lesion, their relationship to the primary motor and somatosensory cortices remained relatively constant. In contrast, stereotactic coordinates are susceptible to the effects of displacement by mass lesions. Defining regions of cortical activation was performed by selecting a t-statistic threshold derived from a previous study in which somatosensory responses to intraoperative cortical stimulation were compared with the strength and location of PET activation. A high t-statistic threshold (t ≥ 4.75) was selected, based on both statistical and biological evidence. Such a threshold has been previously shown to be biologically significant by correlation with intraoperative cortical stimulation. The peaks were statistically significant (p < 0.05). Peaks with t-statistic values less than 4.75 may represent regions of increased focal blood flow and neural activity, and we may, therefore, have underestimated the number of cortical areas activated in all groups. Thus, it would be incorrect to conclude from our study that secondary somatosensory and motor areas are not activated in healthy volunteers (as has been demonstrated in previous activation studies). However, our data indicate that, in comparison with the control studies, secondary sensorimotor areas are more strongly activated in patients with lesions, especially those affecting the central area.

In our study, the limbs opposite the unaffected hemisphere were used in the control studies and, within the statistical constraints discussed previously, yielded results
Motor and somatosensory cortex representation

expected from earlier studies. Some of our motor activation results may have been potentially confounded by ipsilateral or mirror movements. Although close observation ensured the detection of gross movements of the limb opposite to that being studied, the exclusion of finer movements can only be assured using electromyography. The infrequent occurrence (one case) of ipsilateral primary motor cortex activation, however, supports our contention that significant unwanted motor activity did not affect our data. Furthermore, studies in which there is somatosensory stimulation should not be affected by the confounding effects of mirror movements.

Clinical Relevance

A knowledge of the location of eloquent cortex is a prerequisite for safe surgery in the central region, and alterations in the correlation between structure and function are of potential significance in determining the extent of resection. Hence, in situations in which cortical motor and somatosensory representation may be reorganized, an understanding of the patterns of reorganization is necessary. Several studies conducted during this decade, including those by Uematsu and colleagues and Seitz, et al., have suggested that the primary motor cortex may extend anterior to the precentral gyrus and that the hand motor and somatosensory areas may occupy a variable position along the dorsoventral axis of the sensorimotor strip in patients with seizures and/or supratentorial mass lesions.

The use of direct cortical landmarks in our study contrasts with those conducted by Uematsu and colleagues and Seitz, et al. In the former study, two thirds of primary motor responses were located less than 10 mm anterior to the central sulcus, the position of which was estimated using skull landmarks. In the presence of structural brain lesions, this proportion dropped to less than one third; however, no account was taken of the structural displacement of sulci and gyri by the lesion. Seitz, et al. examined six patients with tumors in the precentral gyrus by using functional PET scanning. They described large-scale plasticity of motor representation, such that primary motor activation could be shifted anterior to the precentral gyrus. Their measurements were based on the assumption of morphological symmetry of the central sulcus between the two hemispheres and must, therefore, be interpreted using caution. Although we documented several cases in which peak primary motor activation was localized to the postcentral gyrus and somatosensory activation was localized to the precentral gyrus, no instances of primary sensorimotor cortex located beyond these gyri were observed.

Unlike the current study, Nii, et al., observed great variability in the dorsoventral distribution of hand motor and somatosensory responses. They found that hand motor responses extended 8.5 cm along the central sulcus, which was moderately greater than the 5.5-cm distance observed by Penfield and Boldrey. In contrast, we noted that, in all but one study (somatosensory), hand motor and sensory responses always occurred within or adjacent to the precentral knob. We can, therefore, confirm that the findings of Yousry, et al., in healthy volunteers, also hold true for patients with cerebral lesions, and the anatomico-functional relationship that they described is not altered by cortical reorganization.

Changes in cortical representation, such as the recruitment of other cortical regions in patients with supratentorial lesions, may play a role in functional recovery or the mediation of residual function. Although the effect of resecting these areas in such patients is unknown, evidence from animal studies suggests that, in the presence of preexisting destruction or impairment of the primary sensorimotor cortex, resection of secondary sensorimotor areas may add to the clinical deficit. By providing information on the patterns, anatomical extent, and spatial constraints of altered sensorimotor representation, our data should assist in presurgical planning when function in the central area is to be preserved.

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Address reprint requests to: David C. Reutens, M.D., F.R.A.C.P., Department of Neurology, Austin and Repatriation Medical Centre, Studley Road, Heidelberg, Victoria, 3084 Australia. email: reutens@austin.unimelb.edu.au.